NCI-Frederick
Animal Care & Use
September 2006

Newsletter Contents

ACUC Member Spotlight

Dr. Vincenzo Coppola

Vincenzo (Enzo) Coppola is a Staff Scientist affiliated with the Gene Targeting Facility in the Mammalian Cancer Genetics Program. He received his Medical Degree from the University of Naples (Italy) and his Specialization in Oncology from the University of Padova (Italy). He has been at the NCI-Frederick facility since 1997 when he began as a visiting fellow.

During his career, Dr. Coppola has consistently been using mouse models. For his specialization studies, he employed a model of human lymphoma in SCID mice in which he showed the importance of specific T cell subpopulations in supporting the growth of EBV positive lymphomas. At the NCI-Frederick, he has worked for many years in the generation of knockout and knockin mouse models. In addition, he applies his expertise in gene targeting technology to the study of the role that neurotrophins and their receptors play in the nervous system and other systems.

Dr. Coppola joined the NCI-Frederick ACUC in 2005. He brings to the committee his experience in the generation of genetically modified mouse models. Currently this technology is evolving rapidly and the scientific community in Frederick is extensively using it. In reviewing animal study proposals, he feels strongly that it is of primary importance to optimize the use of the animals. He believes that carefully designed studies in which the maximum information possible is obtained from the animals utilized should be every investigator's priority. Also, he believes that serving on the ACUC is a great learning opportunity that he recommends to all investigators working with animal models.

He and his wife reside in Frederick, which they consider a good place to raise their two children Oscar (4) and Emma (1). Playing and watching soccer fill the rest of his limited spare time.

Revised ACUC Guidelines

The ACUC has recently revised the following guidelines. Please ensure that you and your staff review these guidelines and incorporate into your research study as they apply:

Guidelines Regarding Modifications to Animal Study Proposals [July 2006]

Guidelines for the Designated Member Review and Expedited Review Processes [July 2006]

These guidelines can be found at the following site: **http://web.ncifcrf.gov/rtp/lasp/intra/acuc/fred/guidelines_nci.asp**

Parvoviruses - MVM/MPV

Parvoviruses are small, non-enveloped DNA viruses. They are generally species-specific and several mammals, including man, have one or more parvoviruses associated with disease. Perhaps the most commonly known are those infecting dogs and cats where significant morbidity/mortality resulting from gastrointestinal disease occurs in young puppies and cerebellar hypoplasia occurs in kittens infected in utero or shortly post-partum.

One problem with parvoviruses is their inherent stability to pH, solvents, elevated temperatures as well as other environmental factors. They are highly contagious and remain viable for weeks in urine, feces, and other contaminated materials thus producing significant environmental contamination. Rigorous cleaning/decontamination procedures are necessary to reduce/remove the threat following an outbreak of parvovirus. Since parvoviruses are not enveloped, they are not as susceptible to many routine cleaning/disinfecting agents. Because parvoviruses are a significant veterinary risk, there are several disinfectants specifically labeled as virucidal for parvoviruses. A bleach solution is commonly used to inactivate parvovirus contaminated materials as it is inexpensive and highly active.

Parvoviruses, amongst the smallest known viruses, require actively replicating host cells to generate progeny. Thus, common host target cells are those of the gastrointestinal tract and the immune system. There are two known parvoviruses in mice – Minute Virus of Mice [MVM] and Mouse ParvoVirus [MPV – originally called orphan parvovirus of mice]. MVM has been known for decades. MPV was originally identified in the mid-1980s as a parvovirus that is antigenically distinct from MVM [McKisic et al. 1993]. These two viruses share significant homology in their nonstructural protein genomic

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sequences but there is divergence in their structural protein genomic sequences. Cross protection studies suggesting that immunity to one of the viruses does not provide protection against the other further confirms differences in their structural proteins [Hansen et al.]. Natural infections with both viruses are associated with asymptomatic disease; however, MVM can produce clinical disease under experimental conditions. MPV produces persistent, subclinical infections that can alter immune function and may pose a threat to rodent studies even though the mice appear clinically normal.

Until recently MAP assays conducted at NCI-Frederick tested for the presence of MVM but not MPV. Now that NCI-Frederick is conducting viral screening using PCR technology we can detect MPV as well as MVM. This recently led to finding a positive test for MPV in a vial of Lewis lung mouse tumor cells from the DCTD Tumor Repository. Since historical testing did not evaluate for MPV, this cell line was reported as MVM MAP negative and has been used by various investigators both within and outside NCI-Frederick. The presence of MPV genomic sequences in these cells has been confirmed; however, we have not yet determined whether this is the result of a productive infection with MPV. There are many reports of the difficulty of growing MPV in vitro with successes to date only occurring with activated T-lymphocytes serving as the host cells. Since the positive test was obtained from cells that were in serial in vitro passage, it raises the question of whether these Lewis lung cells are actually infectious when inoculated into mice. Presently, LASP is working to develop further data on this cell sample as well as to develop a means to screen other historically MAP negative samples for MPV. There has not been a change in NCI-Frederick ACUC policies regarding MPV. However, the finding of this positive result does suggest that future MPV testing may find positive assays so we are working to determine what the significance of these findings might be. If you have questions or concerns please contact Mr. Pete Gorelick [301-846-1134], Dr. Jeanne Herring [301-846-5195], or any LASP or ACUC representative.

Hansen GM, Paturzo FX, Smith AL. 1999. Humoral immunity and protection of mice challenged with homotypic or heterotypic parvovirus. Lab Anim Sci: 49(4):380-4.

McKisic MD, Lancki DW, Otto G, Padrid P, Snook S, Cronin II DC, Lohmar PD, Wong T, Fitch FW. 1993. Identification and propagation of a putative immunosuppressive orphan parvovirus in cloned T cells. J Immunol: 150 (2): 419-428.

Animal Study Proposals – IBC Review

All initial submissions, renewals and modifications to ongoing Animal Study Proposals that involve the following require review and approval by the NCI-Frederick **Institutional Biosafety Committee** prior to the release of the applicable ACUC document:

- *Transgenic or Knockout Animal Strains*
- *Recombinant DNA*
- *Transfected Cell Lines*
- *Human or other primate tissues or cell lines*
- *Toxins*
- *Other Potentially Infectious Materials*

All investigators are encouraged to contact the IBC Office in advance if there are any questions regarding possible coverage. This is particularly important in the case of ASP renewals, as the registration requirements may have changed … so while your previous submission three years ago did not require a registration, your renewal may now require IBC review and approval.

If a registration is required, please be sure to promptly and thoroughly respond to the requests required to secure your IBC registration to alleviate any potential delays in proceeding with your applicable ACUC document.

The IBC has recently implemented registration submission deadlines. Please contact Cara Leitch [301-846-7299] or Theresa Duley [30-846-5038] for any IBC related issues or questions.

Rodent Tail Biopsies

The ACUC would like to remind all investigators and animal users that prior to performing tail biopsies on live animals that he/she should refer to the ACUC ***Guidelines on Tail Biopsy for DNA Analysis and/or Genotyping of Mice***. The maximum permissible biopsy collection is 5 mm [without justification authorized by the ACUC in advance]. Investigators are encouraged to take less if possible or to consider alternative collection methods [i.e., ear punch] for DNA analysis/ genotyping. Please contact the **ACUC Office** if there are any questions or concerns. Your cooperation is greatly appreciated.

http://web.ncifcrf.gov/rtp/lasp/intra/acuc/fred/guidelines/Tail_Biopsy.pdf

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